B

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/424,080	02/14/2000	VLADIMIR ZAVIALOV	933-149PCT	7527

7590 02/10/2004

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 220400747

EXAMINER
SCHWADRON, RONALD B

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/424,080	ZAVIALOV ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 12-19* is/are pending in the application.

4a) Of the above claim(s) *12-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/24/2003 and the amendment filed 8/23/2003 has been entered.

2. Claims 1,3-5,19 are under consideration.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1,3-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed wherein the limitation "or during treatment diseases wherein cyclosporins, FK506 or rapamycin can be exploited" has been removed from claim 1 as per the previously pending claim. There is no support in the specification as originally filed for the composition of claim 1 wherein the aformentioned limitation is deleted. The deletion of the aformentioned limitation changes the scope of the claimed invention such that it is no longer supported by the specification as originally filed. There is no support in the specification as orignally filed for the scope of the claimed invention (eg. the claimed invention constitutes new matter).

5. Claim 1 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons elaborated in the previous Office action. Applicants arguments have been considered and deemed not persuasive.

Applicant is in possession of compositions comprising immunosuppressants and bioactive peptides consisting of SEQ ID NO: 1 (also known as alpha-peptoferon), which consists of positions 130-137 of human IFN-alpha, and SEQ ID NO: 2 which consists of variants of SEQ ID NO: 1. Applicant does not disclose any bioactive peptide corresponding to a high affinity binding site/antiproliferative activity other than SEQ ID NOS: 1-2, or any recombinant protein. Adequate written description requires more than a mere statement that it is part of the invention. The sequence itself is required. A description of a genus of peptide or polypeptide sequences may be achieved by means of a recitation of a representative number of peptide or polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Regarding applicants comments, adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. In the instant application, the amino acid itself or isolated protein is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Applicant has indicated that

other examples of the claimed peptides can be produced based on teachings of the specification. However, adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. In the instant application, the amino acid itself or isolated protein is required. Regarding applicants comments, the claimed invention is not limited to art known peptides. It encompasses any peptide with the particular functional attributes recited in the claim.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 1,3,19 are rejected under 35 U.S.C. 102(b) as being anticipated by Gryn et al.

Gryn et al. teach a composition of cyclosporin and interferon alpha (see page 222, second column, wherein the composition is the aforementioned agents in their respective containers). Original claim 5 in priority document FI 972121 indicates that the term composition as used by applicant encompasses physically separated preparations. The peptide recited in the claims is found in interferon alpha. The functional properties recited in the claim are inherent properties of the aforementioned composition.

8. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Yoshida et al.

Yoshida et al. teach a composition of cyclosporin and interferon beta (see page 68, second column, wherein the composition is the aforementioned agents in their respective containers). Original claim 5 in priority document FI 972121 indicates that the term composition as used by applicant encompasses physically separated preparations. The peptide recited in the claim is found in interferon beta. The functional properties recited in the claim are inherent properties of the aforementioned composition.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 3, 5, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gryn et al. in view of Zav'Yalov et al. (Molecular Immunology 1995; 32(6): 425-431; IDS document) and Fish (WO 94/01457).

Gryn et al. teach a composition of cyclosporin and interferon alpha (see page 222, second column, wherein the composition is the aforementioned agents in their respective containers). The peptide recited in the claims is found in interferon alpha. The functional properties recited in the claim are found in the aforementioned composition because the aforementioned composition is the same as the composition recited in the claims. Gryn et al. do not teach SEQ ID NOS: 1 (also known as alpha-peptoferon) or 2. Zav'Yalov et al. teach a bioactive peptide comprising positions 130-137 (i.e. an 8-mer) of interferon-alpha2 (authors definition: alpha-peptoferon) which is a bioactive peptide and displaces labeled IFN-alpha2 from the IFN-alpha2/receptor complex, meaning that it interacts with the high-affinity binding site of IFN-alpha2 (see the abstract and page 425, left column, and page 427, right column in particular). The mouse and human IFN-alpha2 shown in Figure 1 comprises SEQ ID NO: 1 with a single substitution at position 131 from "T" to "R" or "K", respectively which meets the claim

limitation of a variant of SEQ ID NO:1 that is SEQ ID NO: 2, such that one amino acid of SEQ ID NO: 1 is substituted. Fish teaches that interferon alpha derived peptides which bind the receptor for interferon alpha can be used in pharmaceutical compositions (see page 2). One of the peptides disclosed by Fish is a 11mer which contains the peptide of SEQ. ID. No:1. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Gryn et al. teach a composition of cyclosporin and interferon alpha whilst Zav'Yalov et al. teach a bioactive interferon-alpha2 derived peptide which interacts with the high-affinity binding site of IFN-alpha2 and Fish teaches that interferon alpha derived peptides which bind the receptor for interferon alpha can be used in pharmaceutical compositions. One of ordinary skill in the art would have been motivated to do the aforementioned because Fish teaches that interferon alpha derived peptides which bind the receptor for interferon alpha can be used in pharmaceutical compositions and Zav'Yalov et al. teach that loop DE (AKA alpha peptoferin) mediates immunomodulatory activity of interferon alpha (see lasts sentence, page 428, second column, continued on next page).

11. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gryn et al. in view of Zav'Yalov et al. (Molecular Immunology 1995; 32(6): 425-431; IDS document) and Fish (WO 94/01457) as applied to claims 1, 3, 5, 19 above, and further in view of Isoai et al. (Cancer Research 1994 March; 54: 1264-1270).

The previous rejection renders obvious the claimed invention except wherein the peptide is bound to a small molecular or macromolecular substance to increase the stability of the peptide. Isoai et al. teach a peptide chemically coupled to albumin to form stable entities – and the conjugate was more stable than the peptide alone (see the abstract in particular). Further, albumin was chosen because it is the most abundant and stable protein in serum and would increase the half-life of the peptide (see page 1264, right column, paragraph 3 in particular). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Isoai et al. teach a peptide chemically coupled to albumin to form stable entities – and the conjugate was more stable than the peptide alone. One of ordinary skill in the art would have been motivated to do this because the stability of the peptide was greater when conjugated to albumin as taught by Isoai et al.

12. No claim is allowed.

13 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644